



Review

The European Society of Therapeutic Radiology and Oncology–European Institute of Radiotherapy (ESTRO–EIR) report on 3D CT-based in-room image guidance systems: A practical and technical review and guide

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ABSTRACT

The past decade has provided many technological advances in radiotherapy. The European Institute of Radiotherapy (EIR) was established by the European Society of Therapeutic Radiology and Oncology (ESTRO) to provide current consensus statement with evidence-based and pragmatic guidelines on topics of practical relevance for radiation oncology. This report focuses primarily on 3D CT-based in-room image guidance (3DCT-IGRT) systems. It will provide an overview and current standing of 3DCT-IGRT systems addressing the rationale, objectives, principles, applications, and process pathways, both clinical and technical for treatment delivery and quality assurance. These are reviewed for four categories of solutions; kV CT and kV CBCT (cone-beam CT) as well as MV CT and MV CBCT. It will also provide a framework and checklist to consider the capability and functionality of these systems as well as the resources needed for implementation. Two different but typical clinical cases (tonsillar and prostate cancer) using 3DCT-IGRT are illustrated with workflow processes via feedback questionnaires from several large clinical centres currently utilizing these systems. This report whilst comprehensive is not exhaustive as this area of development remains a very active field for research and development. However, it should serve as a practical guide and framework for all professional groups within the field, focussed on clinicians, physicists and radiation therapy technologists interested in IGRT.

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This report from the European Society of Therapeutic Radiology and Oncology (ESTRO)–European Institute of Radiotherapy (EIR) aims to provide the necessary information to meet the needs of radiotherapy professionals interested in applying IGRT solutions. The report is specifically focused on 3DCT-IGRT systems and the process of use of these systems. For the major commercial IGRT solutions, specifications are given which have been updated at the time of completion of the report. However, the focus of this report is on generic rather than on specific manufacturer's issues.

The subject of the report is limited to 3DCT-IGRT systems, referring by this only to equipment situated within the treatment room. This means that planar imaging is not covered, neither as 2-dimensional (2D) nor as orthogonal 2D–2D ('semi-3D') solution. Also the use of flat panel detectors for 2D imaging in systems intended for

3D imaging is not covered, although the possibility exists in some commercially available systems. This definition may limit the scope of the report, but the entire area of in-room IGRT systems would be too comprehensive to be covered in a single report. The subject of 3DCT-IGRT was chosen, as this is the most recent addition to the spectrum of image guidance solutions which is in wide clinical use. This is therefore an area in which many clinics are, presently and in the near future, in the process of purchasing new equipment as well as implementing existing and newly acquired equipment into clinical use.

This report does not attempt to benchmark different solutions, either generically or with respect to commercial availability, nor does it attempt to rank solutions. A comparison is not undertaken with other categories of in-room image guidance solutions but rather the report reviews the principles, limitations, applications, quality assurance and workflow issues related to the limited subject of 3DCT-IGRT solutions. Additionally, the report attempts to establish the use of a standardized nomenclature or glossary in

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the field of in-room IGRT, specifically with regard to 3DCT-IGRT solutions. Such standardization appears to be timely in this subject, as different terminologies are encountered with a variety of implications in the literature. A standardization of nomenclature will act to improve the general understanding of image guidance terms, and to enable consistent and easy communication between the radiotherapy professionals in this field.

The intended audience of this report is the radiotherapy professionals involved in the use of 3DCT-IGRT for instance in the process of purchasing this equipment or bringing image-guided equipment into clinical practice but it will have utility for all groups of professionals within the field, particularly for clinicians, physicists and radiation therapy technologists (RTTs) new to the field of image guidance. The target group is not for professionals already experienced in the use of 3DCT-IGRT techniques and seeking more knowledge in the subject (except for solutions they are not already familiar with). This report does not attempt to answer specific “how to” questions regarding the use of the techniques described, but gives a more general overview of a variety of issues relevant when considering the use of these systems. This being said, the report can hopefully still serve as a comprehensive overview of issues both theoretical and practical with relevant references, glossary and case studies that will be relevant for professionals at all levels of experience.

The report is divided into five main sections following this introduction with several sections of this report (see below) web-linked due to limitations in the journal space. Sections 1 and 2 will inform the reader of the rationale for IGRT and provide background to the general principles for the different options for 3DCT-IGRT. This will be followed, in Sections 3 and 4, by a practical checklist for the issues in image guidance, and a process pathway of two clinical cases illustrated by a questionnaire of radiotherapy centres routinely using 3DCT-IGRT. Finally perspectives of the current state of IGRT will be discussed in the last section:

- Section 1: Rationale and objectives of IGRT. In this section, the clinical potential of image guidance is addressed, with specific reference to the use of 3D image guidance as compared to other techniques.
- Section 2: Principles of 3DCT-IGRT. A short history of CT-based image guidance is given, and the general principles are reviewed for four categories of solutions; kV CT and kV CBCT (cone-beam CT) as well as MV CT and MV CBCT.
- Section 3: General issues concerning 3DCT-IGRT with a checklist. This section includes a breakdown of the workflow of the image guidance processes and outlines potential questions/issues, divided into process topics, to consider when purchasing image-guided equipment. The issues and terms involved for each topic are explained with respect to their implications in the image guidance procedural pathway.
- Section 4: A clinical 3DCT-IGRT radiotherapy process pathway questionnaire is outlined and sent to a selection of centres where its application is in routine use. These centres have completed this questionnaire regarding the use of their image guidance procedure for two different but typical clinical cases. The questionnaire is explained and the answers from the clinics are compiled.
- Section 5: Perspectives. This section is to provide a simplified overview of the current limitation, caveats and difficulties faced with IGRT for clinical use. It will touch on some of the relevant issues for consideration with current IGRT systems and future developments.
- The web-linked sections include the authors' conflict of interest statements; the preface from the EIR; all tables and figures listed in this report; the acknowledgements; [Appendix A](#) provides the answers to the workflow check list from participating

clinical centres including the manufacturer-based specifications for the four major commercial vendors (Elekta, Siemens, TomoTherapy, and Varian) provided by the respective companies for the check list of Section 3; [Appendix B](#) provides the Clinic Questionnaire assessing 3DCT-IGRT process pathway for two clinical cases; [Appendix C](#) provides the responses to the 3DCT-IGRT Clinic Questionnaire; and [Appendix D](#) provides the Glossary.

Rationale and objectives of IGRT

Radiation therapy has experienced a remarkable evolution from its classical 2D approach to 3D techniques that design the treatment based on image-derived 3D models, providing tools to assess and consequently potentially adapt the treatment to response [1]. The introduction of 3D morphological and functional imaging techniques has changed the way target volumes are defined, moving from derived 2D anatomic parameters to customized targets. The subsequent clinical implementation of refined conformal delivery techniques such as IMRT offers the ability to sculpt the dose more closely to the tumour volume. The justification can be readily recited by the practicing radiation oncology professional: “increasing precision and accuracy in radiation delivery will lead to reduced toxicity with the potential for dose escalation and improved tumour control”. However, with this close conformity of the dose to the tumour volume and the rapid dose fall off outside the tumour volume, the accuracy of daily treatment delivery is crucial. It is, therefore, essential that the daily treatment situation is a replica of the patient position and anatomy to that at the time of treatment planning. Inevitably there will be uncertainties introduced in this process and a “safety” margin is added around the tumour volume to compensate for these uncertainties. The International Commission on Radiation Units and Measurements (ICRU) in its Reports 50 and 62 [2,3] created a nomenclature that formalized a principle facilitating the image guidance task by specifying the geometric constructs and margins. This is diagrammatically illustrated in [Fig. 1](#) [4]. These margins explicitly mitigate the technical challenge of co-registering the radiation dose distribution with respect to the tumour and normal tissue within the human body over many fractions of radiation treatment.

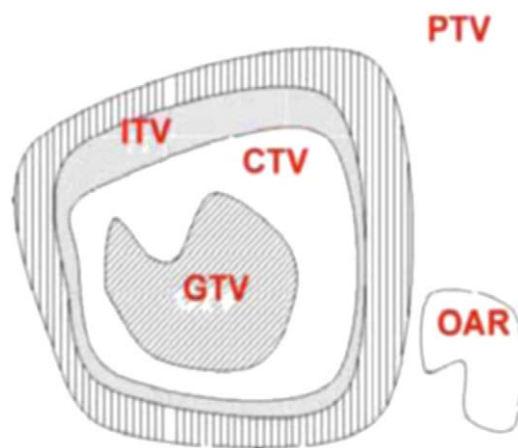


Fig. 1. ‘ICRU volumes’ relevant for image guidance: the gross tumour volume (GTV) is the primary tumour volume, the clinical target volume (CTV) compensates for microscopic disease, the internal target volume (ITV) takes the variations in size and position of the CTV into account, the planning target volume (PTV) compensates for geometric miss and the organ at risk (OAR) is an organ whose sensitivity to radiation is such that the dose received from a treatment plan may be significant compared to its tolerance [4].

Issues of margin reduction

Reduction of margins has become a focus on radiotherapy because margins are directly associated with excess toxicity and lead to constraints on dose escalation for increased control. Moreover, organs-at-risk (OARs) are often close to or overlapping the planning target volume (PTV) thus creating an inherent dose prescription limitation and optimization problem. Various imaging technologies have been integrated with treatment delivery systems to accommodate this particular problem of margin reduction (introducing the concept of IGRT) and are now commercially available [5]. Each of the tools has the potential to reduce set-up errors and hence optimize the contouring of the PTV and OARs.

IGRT aims at reducing geometrical uncertainty by evaluating the patient geometry at treatment and either altering the patient position or adapting the treatment plan with respect to anatomical changes that occur during the radiotherapy treatment course. A first example of successful implementation of combining conformal radiotherapy (CRT) with IGRT (CRT-IGRT) is presented with dose escalation protocols of which prostate radiotherapy is a typical case. Different studies have been published on the localization and the quantification of prostate motion with various targeting modalities. The advances in prostate targeting allow for dose escalation due to the reduction in margins or in a production of a patient-specific margin, which in turn results in improved biochemical control rates, while preventing an increase in rectal and bladder complications [6–8].

Another approach, requiring the same level of accuracy, aims at sparing normal tissue whilst maintaining the same dose in the target volume (conformal avoidance). A typical example of this approach is given in the treatment of head and neck cancer where the challenge resides in the protection of the salivary glands to decrease the incidence of xerostomia (dry mouth syndrome) thereby improving the quality of life [9,10]. In addition, IGRT has initiated the mainstream implementation of stereotactic body radiotherapy (SBRT) high-dose hypofractionated treatments of various types of tumours including inoperable early-stage lung tumours, primary or metastatic liver tumours and those of pancreas, kidney, and spine [11–13]. The accuracy needed for safe daily SBRT treatment is achieved by ensuring reliable and reproducible patient immobilization, planning and treatment correlation, pre-treatment quality assurance using daily imaging and possibly a method of accounting for tumour motion during treatment [14].

Finally, during the course of treatment, deformations and changes of the anatomy are important. Large deformations in cervical cancer were found for which rotational corrections would not be enough, and during head-and-neck and lung tumour treatments considerable volume changes can occur [15–19]. Even if several groups have developed methods to include knowledge of tumour modifications, 3D volumetric imaging could be used to reposition the target volume and to alert the clinician if shrinkage of the tumour, or change in anatomy, might result in an excessive irradiation of organs at risk. In such clinical presentations of the disease, a bony anatomy representation is not accurate enough and a tool dedicated to visualize soft tissue in individual body anatomy is mandatory to allow for adaptations of the treatment plan.

Sources of geometric uncertainties

As IGRT aims at reducing geometrical uncertainty, the optimization of margins is one of its primary objectives. However, there is some evidence in the literature that the technical precision provided by IGRT also induces a potential danger as to reducing margins to levels that are inadequate, for instance because they ignore inherent clinical uncertainty in target delineation [20]. Uncertainties in target localization can occur either in the pre-treatment

stage and are therefore systematically reproduced during treatment, or in the delivery stage varying on a daily basis. In order to appreciate the advantages and limitations of 3D volumetric image guidance systems, a short review of some important sources of these geometric uncertainties is warranted, such as in target delineation, phantom transfer errors (the error accumulated in transferring image data from initial localization through the treatment-planning system to the linear accelerator), set-up errors and physiological changes.

The identification of the target volume is potentially the largest source of a systematic error. Typical delineation errors vary per anatomical site but are rarely below 3 mm [21]. The quality and resolution of the imaging modality and the human factor in outlining (inter- and intra-observer variability) will both affect the tumour volume identification and introduce variability. Multi-modality imaging and the ability to co-register images have the potential to improve tumour volume identification [22–24], however, the gain is dependent on tumour site, the method of imaging and the quality of registration algorithms.

Phantom transfer errors are created when moving data through the planning and treatment process, i.e. acquiring the patient data at CT planning and then transferring, via the treatment-planning system and ancillary equipment, to the linear accelerator. They can be evaluated by scanning a phantom, producing a plan, generating digitally reconstructed radiographs (DRRs) and comparing them with electronic portal images (EPIs) to assess if the delivered plan matches the planned treatment.

Set-up errors occur when the position and the anatomy of the patient at the planning CT is not reproduced accurately on treatment [25]. There are two types of set-up errors, systematic and random. Systematic errors are reproducible consistent errors, occurring in the same direction and of similar magnitude over the course of treatment. Individual systematic errors can be represented as the distance of the mean of the daily positions to a pre-defined ideal point in space. A random error, as its name suggests, varies in direction and magnitude from day-to-day and is represented by the range of different positions for each delivered treatment fraction. An example of this is shown in Fig. 2. Factors affecting the accuracy of set-up include the site treated, immobilization and positioning methods used and the patient's condition. The average values of the systematic (Σ) and random (σ) set-up errors for a group of patients can be used to define a CTV-PTV margin.

Physiological changes occur during the course of radiotherapy. Not all organs move the same hence deformation is present. Examples are prostate motion with respect to the bony anatomy, tumour shrinkage or progression during RT, (breathing) motion in lung and breast tumours, and random deformation of the neck [26–30]. Like set-up errors these changes can be systematic and random. Volumetric imaging can visualize the organ or target but often with great effort. One way to overcome this is the use of fiducial marking the area of interest but it is limited in assessing the degree of deformation. In case of deformations affecting the dose to target or organs at risk, adaptation of the treatment plan during the radiation might be needed.

Reducing set-up errors – image verification

Reproducing the patient's position by aligning skin marks and room lasers only, inevitably introduces errors because skin is mobile. Electronic portal imaging devices (EPIDs), providing 2D images and bony anatomy information for verification, improve the set-up accuracy. These images can be acquired prior to treatment delivery to be evaluated retrospectively: 'offline verification', or prospectively: 'online verification'. Offline verification aims to eliminate any systematic error between planning and treatment averaging the patient's individual set-up error over a number of

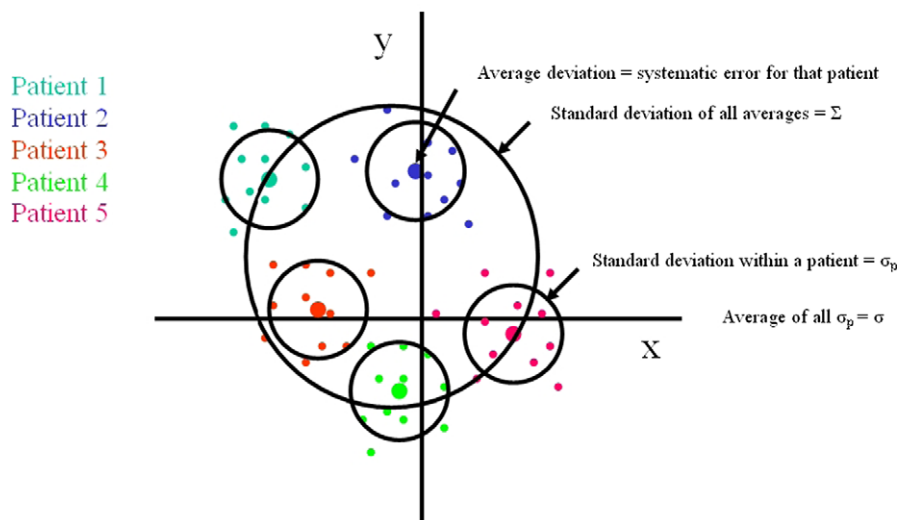


Fig. 2. Graphical presentation of systematic and random set-up errors of a group of five patients. Note the patient's error for each measurement in small coloured dots, the average systematic error per patient in large coloured dots, the standard deviation of the set-up error within a patient in small circles and the standard deviation of all averages in the large circle. The figure illustrates that detailed knowledge of the set-up error of a given patient can therefore reduce the required margin compared to margins based upon group statistics alone. (Courtesy Peter Remeijer, The Netherlands Cancer Institute, Amsterdam, The Netherlands.)

days, and adjusting the treatment couch to correct on subsequent days. Strategies regarding frequency of imaging and corrective actions have been investigated to derive protocols that maximize the efficiency of EPI in detecting and eliminating systematic errors [31–33]. Online verification allows the possibility of intervening and correcting the set-up prior to treatment delivery, on a daily basis eliminating both random and systematic errors, or in a protocol to eliminate systematic errors. The challenge with this approach is minimizing the time the patient is on the treatment couch while the images are analyzed, a decision made and corrections performed. This approach requires to be integrated smoothly in the treatment chain with automation of the verification and correction process [34].

Using planar imaging techniques such as EPI for bony anatomy set-up assumes a stable relationship between bony anatomy and tumour position. However, this is not always the case, which has quite clearly been demonstrated in patients treated for prostate and lung cancer. The alternatives include using implanted markers to identify the position of soft tissue or use of soft tissue imaging based on 3D information for example in-room CT, cone-beam or MV CT, or in-room MRI. 3D soft tissue imaging has the additional advantage of allowing identification of anatomical deformations during the course of radiotherapy treatment. Random errors can arise from changes in target position and shape between fractions and during treatment delivery.

In lung cancer, anatomical changes during the course of radiation therapy can cause the tumour to shift out of the intended dose region necessitating re-evaluation of the treatment plan [30]. The motion in head and neck cancer is even more unpredictable as oedema, tumour shrinkage and changes in the head and neck posture all influence the position of a given volume in the patient differently [27,35], leading to significant dose changes in the OARs compared to the calculated treatment-planning dose. To accurately control or adapt the radiation delivery, frequent imaging in treatment position including target and organs at risk is needed. Gradual changes, for example tumour regression or oedema, can be assessed offline, while corrections for random shape changes require on-line imaging. The treatment plan can then be adapted and delivered in following fractions. However, CTV to PTV margins not only account for set-up and organ motion but delineation uncertainty has always been intrinsically included. It is rare that

the magnitude of delineation variation is below 3 mm and frequently it is above this level [21,36–39]. Therefore geometrical miss of the target, specifically with smaller margins than 5 mm are inevitable [21,39]. Despite these marginal recurrences for instance in head and neck cancer are rare. This could be explained by overtreatment in dose and size of the high dose region, or over-estimation of the actual tumour size [21,39–41].

Radiation therapy evolved from 2D to 3D in the treatment-planning process, in the same way a similar evolution can be observed in IGRT. DRR and EPI for planning and verification have replaced radiographic films. Simultaneous acquisition of multiple planar images has been automated to provide 2D–2D set-up verification and corrections using a robotic treatment couch, even allowing for breathing synchronization. These techniques, however, share the common limitation in that they cannot visualize the tumour volume or its spatial relationship to surrounding healthy tissues without the help of fiducials such as bony structures or implanted radio-opaque markers. Volumetric imaging techniques nowadays provide the soft-tissue contrast required for daily positioning, providing online information concerning organs at risk as well as tumours and identifying anatomical changes during the course of radiotherapy.

Principles of 3D CT-based image guidance

In principle, 3DCT-IGRT solutions can be categorized by two major classifiers, namely beam quality, i.e. whether they are based on megavoltage or kilovoltage beams, and beam collimation, i.e. whether they are cone-beam or fan-beam solutions (the former uses an open beam and large-area flat panel detector, whereas the latter applies a linear array of detectors in combination with a fan beam). The combinations of these yield four distinct solutions which are commercially available and widely used (Fig. 3):

1. Kilovoltage fan-beam CT (kV CT, commercially available as a peripheral solution by Siemens termed CT-on-rails).
2. Kilovoltage cone-beam CT (kV CBCT, commercially available as integrated solutions for Elekta and Varian linear accelerators (linacs).
3. Megavoltage cone-beam CT (MV CBCT, commercially available as an integrated solution for Siemens linacs).



Fig. 3. Commercially available CT-based image guidance systems. (A) Siemens CT-on-rails; (B) Elekta kV CBCT (Synergy); (C) Varian kV CBCT (OBI); (D) Siemens MV CBCT (Artiste); (E) TomoTherapy MV CT.

4. Megavoltage fan-beam CT (MV CT, commercially available as the integrated TomoTherapy solution).

A brief history of 3D CT-based image guidance

Historically, the development of CT-based image guidance started in the 1980s, shortly after CT as a technique for 3D X-ray imaging had been developed. CT was invented by Hounsfield and McCormack as a tool primarily intended for diagnostic purposes. The CT image in effect maps the beam attenuation coefficient in the patient in 3D in voxels with high spatial accuracy. Each type of tissue appears distinctly with different contrast in the image owing to the variations in beam attenuation in differ-

ent tissues, and each voxel in the 3D image is assigned a Hounsfield unit (HU) relating to the beam attenuation coefficient. It was soon found that this was very useful, not only for diagnostic work, but also for planning of radiation therapy. The 3D image could be used to identify the target in the patient accurately for beam set-up, and moreover, the HUs gave information on electron density distribution in the patient, readily useful for calculation of the absorbed dose in the patient. The process of using CT images for treatment planning, including both delineation of relevant anatomical structures, beam set-up, and calculation of absorbed dose, was soon automated in computerized treatment-planning systems (TPS) of which the quality is constantly being increased.

Kilovoltage fan-beam CT (kV CT)

Use of in-room diagnostic CT as a way to localize the patient in the treatment room just prior to a treatment fraction was first suggested by placing a CT-scanner inside the treatment room [42]. The advantage over planar imaging for localization and verification is obviously the availability of 3D information and the visibility of soft tissue in the CT-scan. With the CT-scanner in the treatment room there is only one couch for the patient. There are two methods of acquiring the CT image for the patient set-up, either with the treatment table of the actual treatment linac, where the patient on the treatment couch must be moved between the scanner and the treatment unit, or with the CT-scanner (and/or the treatment unit) moved to/from the patient. This introduces the sources of error, in terms of the tolerance of the motion of the system itself, or the inherent separation of imaging and treatment isocentre of the patient reacting to being moved and of the time taken to move the patient or the equipment.

Kilovoltage cone-beam CT (kV CBCT)

The problem of patient movement after imaging can be obliterated if a gantry-mounted X-ray source can be used for the production of CT images. During the last 5 years the technology of linac-integrated cone-beam-CT (kV CBCT), first introduced by Jaffray et al. [43], has matured and reached a widespread clinical application [44–47]. The imaging components, a conventional CT X-ray source and flat panel detectors, are mounted to the linac gantry. In two current commercially available systems the imaging axis is chosen at a 90° angle with the treatment beam; an in-line geometry by a third vendor is announced to be available soon.

Megavoltage cone-beam CT (MV CBCT)

Feasibility studies on in-room MVCT scanning were performed in the 80s and were typically based on a single slice tomogram per gantry rotation [48]. A major problem with these approaches was accurate table indentation using the treatment couch. Nakagawa et al. proposed to use a single pre-treatment MV CT slice to verify the patient set-up for stereotactic radiosurgery of the lung [49]. To overcome the problem of table indentation, Mosleh-Shirazi et al. [50] reported a feasibility study on 3D MV CBCT using a scintillation detector – CCD camera-based EPID on the linac, with the image frame acquisition synchronized with the radiation pulses. Pouliot et al. have reported on the clinical feasibility of this approach [51] and recently the vendor has introduced an ‘imaging’ carbon target in the beam line replacing the treatment high-Z target to reduce beam energy to obtain an increased image quality. A review on EPID has been produced by the American Association of Physicists in Medicine [52].

Megavoltage fan-beam CT (MVCT)

With the helical tomotherapy solution (see this section to follow), a concept was introduced using the ring MV gantry for helical fan-beam MVCT imaging just prior to treating with the same gantry [53]. This is now the most widely used solution for in-room MVCT imaging.

General advantages and limitations of kV solutions

The generic principles including hardware, workflow advantages and limitations of the different categories of CT-based image guidance solutions will be covered here. Three dimensional kV-imaging of the patient in treatment position directly prior to treatment is one of the most common 3D IGRT procedures currently

performed in clinical practice. Its main advantage to 3D-in-room MV-imaging techniques is an enhanced image contrast for soft-tissues achievable with low to moderate imaging doses, owing to the prevalence of photoelectric absorption interactions at low energies [54]. This feature not only allows for improved patient set-up accuracy but also ultimately aims to achieve a perfect alignment of the target volume within the reference frame of the treatment beam. However, as the imaging beam and the treatment beam have different sources, alignment of treatment beam and imaging beam is not inherent in these solutions, and has to be established and verified in each set-up. This requires additional quality control relating to both the dosimetry of the imaging beam and its geometry.

There are two categories of 3D kV-imaging solutions currently used in clinical radiation therapy. First, the so-called CT-on-rails technology was developed [55–58]. It consists of a standard diagnostic CT gantry mounted in the treatment room. The second, widespread technical solution refers to linac-integrated kV-imaging equipment, consisting of a diagnostic X-ray source and a flat panel electronic imaging device [43,55–58]. In the following we will briefly describe the main features of these technologies including hardware, workflow, advantages and limitations.

CT-on-rails/in-room CT

First, the technology requires that the treatment room has to be sufficiently large to accommodate a CT-gantry in addition to the treatment linac. For practical reasons, two possibilities for the geometry of the set-up are applied: the rotation axes of linac and CT gantry are either parallel or at a 90° angle. In both cases the patient set-up is performed on the treatment couch at the linac before the treatment table is moved into its imaging position. Next, CT-imaging is performed while the CT gantry is sliding over the static patient couch. After reconstruction of the images the patient is moved back into the treatment position and a registration of the actual 3D-images with the planning CT scan is used to perform the optimal patient set-up of the day.

The achievable set-up accuracy of the indicated workflow crucially depends on the geometrical registration of the CT images within the isocentric reference frame of the linac. The reference target point according to the treatment plan can be determined in the CT image by radio-opaque markers that were previously fixed at tattoo marks on the patient's skin. Furthermore, stereotactic localizers can be used for this purpose.

The main advantage of the CT-on-rails technology is its excellent image quality, which is unrivaled by any other 3D in-room imaging approach [59]. This advantage arises from the use of an imaging fan beam (reduced scatter) in combination with highly efficient standard CT detectors. High contrast CT images of diagnostic quality can be acquired at low additional patient dose such that registration with reference planning CT scans and applications for potential IGRT re-planning strategies are facilitated, e.g. the obtained Hounsfield units can be directly used for reliable dose calculations.

One limitation of the CT-on-rails technology is that by design it cannot be used for the detection of intra-fractional patient or organ motion. Another concern is that minor undetectable set-up errors might be caused by the required movement of the patient between imaging and treatment [60]. The various steps of the workflow may also limit the throughput efficiency of this method.

Linac-integrated kV CBCT

The acquisition of a number of CT projections (for instance 330–720) is accomplished in either full-scan or short-scan mode and takes between 1 and 2 min. Reproducible mechanical instabilities

of the system can be accounted for within the image reconstruction. Simple quality assurance measures guarantee a very precise geometric co-registration of the kV CBCT with the treatment isocentre [61]. The kV CBCT technique is clinically well established. Various reports about QA procedures, the achievable image quality and the related imaging doses are available [59,61–64].

Based on its hardware components the achievable image quality is compromised in comparison to diagnostic CT images. The combination of an imaging cone-beam with an EPID detection system inevitably leads to intensified scatter artifacts in 3D kV CBCT images. Furthermore, motion artifacts caused by breathing or peristalsis during the enhanced scanning times can compromise the image quality. However, scatter correction methods were developed to solve the problem of scatter artifacts [65,66] e.g., a calibration of Hounsfield units, suitable for accurate dose calculations, seems to be feasible. Specific calibration and image reconstruction tools warrant sufficient image quality for a wide range of IGRT procedures at moderate doses [59,62,63,67]. The use of this technique, primarily designed for the correction of inter-fractional set-up errors, is to some extent also suited for the management of intra-fraction organ motion using the same equipment. Fluoroscopic imaging and the acquisition of 4D-CBCT scans have been reported [68–70].

General advantages and limitations of MV solutions

Based on physics arguments the main advantage and disadvantage of megavolt imaging systems can be summarized as follows: as the actual treatment beam is used for imaging, MV-based solutions provide the most accurate (i.e. direct) geometric information concerning alignment of treatment beam and target. On the other hand, MV-based solutions will inherently be inferior to kV-based solutions as the latter provide better soft-tissue contrast owing to the prevalence of photoelectric absorption interactions. MV-based volumetric imaging features some additional generic advantages. The imaging dose can relatively easily be incorporated into the dose calculation algorithm because an MV beam is used for treatment and imaging. An interesting feature of MV CT is the linear relationship between electron density and megavoltage HUs due to the dominance of Compton scatter as the attenuation mechanism for clinical megavolt beams (4–6 MV) for the tissue materials encountered in clinic [71,72]. Moreover, MV-based CT images can be used to complement or even replace diagnostic kV CT images when high density objects introduce severe artifacts, due to the fact that these artifacts and beam hardening are less critical for MV sources. A potential argument against MV-based solutions could be patient dose, however, it should be noted at this point that extra patient dose due to IGRT is a complex issue and the reader is referred to a report on this topic by the AAPM TG 75 [73].

MV CBCT

This concept has been inspired by the wide clinical implementation of EPIDs [52]. Application of the EPID to generate MV CBCT has the advantage that no additional hardware is required. MV imaging using an MV X-ray source and detector is technically simple and robust. The alignment of target and treatment beam is straightforward as the actual treatment beam is used to generate the images. The 3D reconstruction volume acquired with MV CBCT enables to verify and correct patient set-up in the linac coordinate system and compare the treatment patient position with the planning patient position as defined by the planning CT.

A major concern in MV CBCT is the dose outside the target (concomitant dose) introduced by the target localization process due to the challenge posed by the poor detection efficiency of X-ray detectors in the MV energy range. This low efficiency results in poor signal-to-noise performance for clinical acceptable doses. A

first prototype for 3D MV CBCT using a scintillation detector required approximately 40 cGy and 2 h reconstruction time on a Sun SPARC 2 to obtain a density resolution of 2% and spatial resolution of 2.5 mm [50].

Several researchers have demonstrated MV CBCT by the use of standard linacs and EPIDs [74,75], and initially resolution was maximized by the use of experimental equipment or application of high doses. Current “low dose” solutions are possible with frame acquisitions during beam-off and a special triggered acquisition mode to maximize signal-to-noise ratio and avoid beam-pulse artifacts [51]. This synchronized mode is triggered directly by the linac. These investigators showed the possibility of using a standard linac with stable low dose rate and an EPID to obtain clinically useful images, and in fact reported the first image acquisitions in a clinical setting [51]. Other strategies for dose reduction include more sensitive detectors [76] or reduction of imaging volume [77,78].

Most approaches to MV CBCT reconstruction assume fixed isocentric geometry and a fixed source–detector relationship. These assumptions might be weak when applied to MV CBCT data acquired on a linac gantry, because the system is not rigid as the MVCT approach. Therefore, this approach requires a correction to be included in the reconstruction algorithm. One such example in the literature reports vertical sag of more than 15 mm between gantry angles of 90° and 270° due to additional weight of a flat panel detector within an ‘experimental’ set-up [51]. At first hand, a deviation of 15 mm from the ideal imaging geometry may present an extreme value. However, it needs to be borne in mind that it is not the absolute value of this deviation which is of vital importance but rather that the observed gravitational sag is reproducible and stable over QA-relevant time scales. As long as the non-ideal irradiation geometry is stable in time, the devised calibration methods can reliably correct for any related artifacts in the cone-beam CT images. To eliminate the need for measuring the physical parameters for each gantry angle, the geometrical factors relevant for MV CBCT acquisition are measured and defined in a series of transformations that are determined by a simple calibration procedure. Projection matrices can then be introduced to be directly used in the filtered back-projection algorithm. Pouliot et al. [51] demonstrated the use of a cylindrical phantom with 108 radio-opaque spheres embedded in a unique helical pattern to perform the geometrical calibration. This procedure includes source-detector distance, detector plane orientation, gantry and detector sagging, and image distortion. The same group also reported the possibility of using the beam parameters to generate a composite plan in the regular TPS combining the MV CBCT dose distribution with the planned treatment dose distribution [79].

MV CT

The helical tomotherapy (TomoTherapy Inc.) approach is an example of an integrated system [53,80] where the concept of an add-on sequential tomotherapy [81–83] device has been combined with helical CT-scanning resulting in a 2-in-1 concept. The continuously rotating gantry combined with a CT-detector array system allows MVCT imaging and can, in principle, be used for *in vivo* dose transmission measurements for dose verification. Basically it is a CT-scanner where the diagnostic X-ray tube has been replaced with a 6 MV linac and the collimating jaws (or shutters) replaced with a binary collimator consisting of small high-density metal leaves. In a way similar to diagnostic helical CT, the patient is treated in slices by a narrow photon beam. CT-image acquisition, using a somewhat lower energy than for treatment, is accomplished with all leaves open prior to treatment.

As the imaging system is integrated with the treatment system (the same beam delivery device and couch synchrony) the MVCT acquisition and geometric QA are inherently included in the treat-

ment delivery QA; the latter being far more important and sensitive to small errors. Opposed to the MV CBCT system, where geometric uncertainties need to be corrected in the reconstruction algorithm, these uncertainties are physically/mechanically minimized in the MVCT approach. Examples of QA issues include field width, collimator twist, MLC centering, isocentre constancy with rotation, couch velocity and accuracy, and synchrony with the gantry rotation. A nice overview of typical QA procedures is given by Fenwick et al. [84]. The issue of image registration accuracy (kVCT versus MVCT) has been investigated by Boswell et al. [85] and Woodford et al. [86]. The latter performed a study investigating the influence of different image acquisition settings on set-up accuracy and consistency in order to optimize these settings in a clinical environment.

General issues concerning CT-based image guidance; a checklist

In the following section, a range of general issues of consideration for CT-based image guidance will be introduced. This will be followed by a list of factors to consider when purchasing equipment. The factors are presented as potential questions you should ask yourself, with the relevance itemized below each question. These questions are listed in order of workflow. The range of issues contributing to the workflow includes:

1. Image acquisition – positioning the imaging device and all preparation necessary for acquiring the image.
2. Image quality and processing – the process after the completion of the image acquisition to the image being available for registration. This also includes assessment of image quality.
3. Image registration and set-up evaluation – the process and methods available to match the acquired image to the reference image; how the corrections are displayed and the methods available for set-up correction and subsequent verification.
4. General factors such as data handling, dose and QA.
5. Clinical implementation.

It is essential, however, that this list is not used solely to base decisions; a visit to observe the equipment in a clinical setting is recommended. The specification and answers from each major manufacturer of equipment can be found in [Appendix A](#).

Image acquisition

When acquiring CT images, several parameters relating to the acquisition must be defined. For all solutions, the field of view

(FOV) must be set according to the desired image extent. The FOV is limited in the longitudinal direction for CBCT solutions, but not for the fan-beam solutions where the patient is moved with respect to the beam throughout the length of the chosen FOV (currently the TomoTherapy Hi-Art system supports scans up to 160 cm in the cranio-caudal direction). The lateral FOV is limited by the size of the detector array, but for the CBCT solutions, the array may be displaced for so-called offset “half-fan” scans extending the lateral FOV.

For fan-beam solutions, the longitudinal spatial resolution must be set via a slice thickness combined with a pitch magnitude, while for the cone-beam solutions, the longitudinal spatial resolution is given by the detector array resolution combined with the source-patient-detector distances. The spatial resolution in the two other directions is given solely by the detector resolution and set-up geometry for all solutions. Insertion of a bow-tie filter, which works for optimal image quality by counteracting the variation in patient thickness in the lateral direction, may be required. For offset geometry, a half bow-tie filter may be available. The rotation arc required for reconstruction of images may be variable both in the fan-beam and in the cone-beam solutions, whereas in the cone-beam solutions also the number of projections over the rotation arc may be variable. The factors for consideration in image acquisition and its relevance are listed in [Table 1](#).

Image quality and processing

The image quality is first of all very different for the kV and the MV solutions, owing simply to the different physical radiation-matter interactions prevalent for the different beam energies. For the kV solutions, the image quality can furthermore be very dependent on the choice of energy within the kV spectrum and the tube current; these should be chosen appropriately depending on the imaged object, whilst these parameters are fixed for the MV solutions.

The 3D images are produced through a computerized reconstruction process for all solutions. Different reconstruction algorithms may be optimal depending on the geometrical set-up and choices of beam parameters. For the cone-beam solutions, the image is reconstructed in a volume, which gives a high resolution in the longitudinal direction obtained through reconstruction, whereas for the fan-beam solutions it is reconstructed in slices and the longitudinal resolution is given by the scan settings.

The image quality may not be the same in the entire FOV, owing to artifacts arising from high-Z materials (for kV solutions), from beam hardening, blurring/averaging over several materials and material boundaries, and image distortion due to the geometric

Table 1

Factors for consideration in image acquisition and their relevance.

What field of view (FOV) length is available in the cranio-caudal direction?
Determines the length of scan available and possible solutions if longer scan lengths are required
What size is the reconstruction circle?
Determines the lateral FOV
Are filters required? – Which filters are available?
Involves time to select and insert, and affects image quality
Are filters interlocked?
If not, then risk of poor quality or unusable scans from incorrect filters selection
Can panel be positioned remotely? If so, does this the system come with an anti-collision system?
Will involve time to position if not remotely accessed
What are the available rotation speeds?
Determines the acquisition time
What are the possible angles of rotation?
Affects the flexibility of scanning; e.g. the possibility of performing half-scans for small regions, rotations through 180 degrees (underneath the patient) and using preset or flexible start and stop angles
How ergonomic is the operation?
One- or two-button operation, foot- or hand-control, several screens affects the ease of operation and the risk of aborted scans
Can the scan be stopped and restarted?
Will result in extra dose if the scan is interrupted inadvertently, and has to be started from the beginning
Also allows the scan to be acquired with the patient in several breath holds.

set-up and motion. The factors for consideration in image quality and processing and their relevance are listed in Table 2.

Image registration and set-up evaluation

When an image has been acquired, the next step is to match it to a reference image (typically from the treatment-planning system), with the purpose of performing necessary patient set-up corrections and/or verifying the patient position. Vendors of IGRT solutions provide software for image registration and matching to reference images tailored to the technical capabilities of the image guidance system. All these software systems contain a set of tools for import of the reference image, matching with acquired set-up images and assessment of the quality of the registration.

Matching may be performed manually or automatically, and a number of choices may be available for filtering of the automatic match procedure. Typical parameters, which can be varied, include the volume or region of interest (ROI) that the registration is performed for a range of HUs to consider for the match, the number of degrees of freedom in the match (translational and rotational), and the centre of rotation. It is important to emphasize that these parameters may have a large influence on the result of the registration and consequently on the set-up accuracy. The user is advised to become acquainted with these issues before initiating clinical applications. It may be possible to perform a non-rigid registration, where deformation of the image is allowed, which can be done in a

number of different ways. These tools are currently under development as discussed in chapter 6 and not yet commercially available at the time of writing this report. Typical tools for the assessment of a match can include spyglass, toggle function, checker board, complementary colours, blending, and measurement tools (for instance a ruler). The match result in terms of magnitudes of variations in the included degrees of freedom can be manually or automatically transferred to a change in the set-up of the patient. The resolution of the set-up variation is dependent on the resolution in the match software and on the capabilities of the set-up equipment (for instance resolution in possible couch movement). The importance of this visual evaluation cannot be overemphasized and the user is encouraged to assess the accuracy of these automated registration tools for a variety of clinical applications. The factors for consideration in image registration and set-up evaluation and their relevance are listed in Table 3.

General factors – data handling

It is important to know whether it is possible to reconstruct and review images acquired, and to perform/assess matching in an off-line environment, or whether this is only possible online (immediately after image acquisition). There may be differences in how and which data are stored – for instance whether raw data or reconstructed data are/can be stored locally or remotely. This will determine the amount of storage space required and how the data can

Table 2

The factors for consideration in image quality and processing and their relevance.

What criteria are given for low contrast sensitivity and image resolution?
Determines the quality of image particularly for soft tissue definition
What reconstruction algorithms are used?
Different types of algorithms may affect speed and image quality
How long does reconstruction take?
If online verification is required the image is needed instantaneously
Is the image quality consistent over the entire field of view?
Affects image quality when a large FOV can be used, e.g. because there is more scatter when using a large FOV

Table 3

The factors for consideration in image registration and set-up evaluation and their relevance.

What functions are available for registration?
Whether the registration is performed over the entire image or a ROI, choice of intensity levels, and soft tissue or bony anatomy selection is available
Selection will affect match results
Is manual or automatic match available?
Affects time to match, training, decision making, and match results
Affects training and ability to check registration
Is rigid- or non-rigid-matching used?
Non-rigid analysis may be useful for 'non-rigid' tumour sites (for example head and neck, bladder or liver patients)
How long does the match take?
Contributes to the time and affects the workflow if online verification is required
What assessment tools are available?
Possibility to view several planes, and availability of visual methods to compare image to reference (spyglass, colourwash, checker board, toggle function)
Affects training and validation of registration process
How are match results displayed?
For example what decimal places, the units of measurement, are used?
How many degrees of freedom are available?
Possibility to select a specific direction for correction, and the centre of rotation (isocentre or reference point); affects translations
Availability of inclusion/exclusion of rotation
Will affect the flexibility of the system, the ability to use different correction protocols, and the precision of the match results
Can the couch correction be applied remotely?
Affects efficiency of on-line verification and correction
If the couch can be moved remotely, is visual monitoring available and/or collision detection systems? Is the movement mechanically limited?
Affects patient safety
What is the resolution of couch movement?
Affects accuracy but is also dependent on couch calibration
Are the images stored to register off-line, and/or is secondary access available?
Will restrict off-line verification process if not available
How is post correction verification performed?
Affects workflow

be used. Also, some of the imaging system software solutions are integrated with the treatment-planning system and/or the treatment machine management, while others are stand-alone systems. The factors for consideration in data handling and their relevance are listed in [Table 4](#).

General factors – imaging dose

Typically, the imaging systems come with a number of pre-programmed protocols for image acquisition. These may be specifically intended for imaging of different parts of the patient with different image qualities. Also, it may be possible for the user to specify settings not included in a pre-programmed protocol, and to programme user-defined protocols. Different settings/protocols will involve different exposure of the patient to imaging dose, and the system will often give an estimate of the dose, e.g., for the kV systems through a CTDI (CT dose index) value [87]. Specifically for the MV systems, the imaging dose inside the patient can potentially be incorporated into the treatment dose already at the treatment-planning stage, if it is the same beam as the treatment beam which is used for imaging. For the 3D images obtained in CT-based image guidance, there is furthermore the possibility of using the images for dose recalculation with the specific patient set-up. This requires reliable HUs in the image for the kV solutions, and for all systems it involves a time-consuming process, which is not easily feasible in an online environment. The factors for consideration in imaging dose and their relevance are listed in [Table 5](#).

General factors – quality assurance (QA) and calibration

Geometric and dosimetric quality assurance and calibration are important both to ensure correct patient set-up and set-up verification, and to optimize the image quality. For solutions where the treatment beam is also used for imaging, the geometrical alignment between the imaging and the treatment systems is inherent. However, for the systems with a separate imaging

beam source, it is of great importance to perform and maintain a good alignment and possible compensation of alignment error within the system.

For all systems, it is important to avoid unnecessary image distortion and artifacts due to poorly calibrated detector arrays. The imaging systems may come with specialized quality assurance phantoms and guidelines for quality control procedures, the use of which can enhance the accuracy and precision of the imaging system. These should be considered a guide to the user, but should not necessarily be considered complete and exhaustive. The factors for consideration in quality assurance and calibration and their relevance are listed in [Table 6](#).

General factors – miscellaneous

There are many other considerations when implementing IGRT and further issues involved include the following items.

- *Bunker size required.* For instance, for the CT-on-rails, a large room is needed, while for the kV and MV CBCT on-board solution there is no extra requirement.
- *Radiation shielding required.* For the MV solutions, the exposure related to the imaging process needs to be incorporated into the calculation for shielding of the room/machine. For the kV solutions, there is little extra requirement, as the units are already situated in the same room as a MV treatment machine.
- *Life span of the equipment.* Both the life span of the detector and the beam source systems should be considered. Specifically for the MV systems, the source is identical to the treatment beam source, so special considerations may exist.
- *Risk assessment of operation of the equipment.* A risk assessment should include a range of features including among others: collision protection, the interlock level of operation, the stability of the system, the automation level, the intuitiveness of operation, the storage of data, the radiation protection, and how ergonomic the operation of the equipment is.

Table 4

The factors for consideration in data handling and their relevance.

Can original images (raw reconstructed) be saved?
Affects the possibility of binning frames
What is the capacity of the hard drives?
Necessary for image storage
Does the system provide an efficient back-up and retrieve procedure?
Affects the analysis and storage of data
If more than one machine is used, are databases shared?
Ability to image patients using the same matching parameters on different linacs; for example on service days
Can the image system be integrated into PACS?
Provides storage solution and network capabilities
How are reference images imported?
Affects the workload and may introduce risk of error. This will depend on treatment-planning systems used
Integration with record and verify system?
Affects safety issues in potentially selecting different patients in the treatment software and the imaging software databases, or selecting different isocentres where multiple isocentres are used

Table 5

The factors for consideration in imaging dose and their relevance.

What CTDI doses are involved for site specific bony anatomy imaging and soft tissue imaging?
For example head and neck (bone), chest, pelvis (bone), pelvis (soft tissue)
Determines the dose received by the patient for bony anatomy and soft tissue imaging
Can the dose be incorporated into planning?
Ability to add concomitant dose to the prescription
Can the images be used for recalculation?
Hounsfield units/CT-numbers must be reproducible and independent of protocol or patient size
Is there a dose record per patient?
Availability of a method of recording dose received by individual patients
If images can be used for dose calculation: is there a QA programme for measuring the stability of the images to perform a proper dose calculation?
Affects accuracy of dose calculations

Table 6

The factors for consideration in quality assurance and calibration and their relevance.

Are phantoms provided for calibration and QA?
Resources and staff available to implement QA procedure
What does the QA procedure entail?
Time necessary for calibration/QA
What is the geometric stability?
Determines how often the QA should be undertaken and the resources required to incorporate into clinical day
How often is calibration required?
This will reduce the possibility of ring artifacts, which are detrimental to the quality of the image
How is alignment between imaging and treatment isocentres ensured?
Incorporation of automatic procedures of correction can enhance precision of the system
Is there a QA tool for verification of consistency in HU?
Important if images are used for dose calculation

- **Audit.** It is appropriate and necessary that an audit system should be established to evaluate the process of image guidance implementation.

Clinical implementation

The previous sections present the process of acquisition and registration to determine the accuracy of the patient set-up. Once the process has been established, responsibilities and specific areas of the process need to be considered for successful complete clinical implementation. These include:

- Managing the process.
- Defining protocols.
- The professionals responsible for making decisions on actions to be taken. This may be a site-specific team or part of the general responsibilities.
- A training and competency framework to ensure that the professionals are confident particularly when making on-line decisions.
- The balance between the number of professionals who are competent and the workload to ensure that both an efficient process and competency are maintained.
- Selection of sites or situations requiring imaging and the resources available, for example, the number of CT-based image guidance linacs.
- The time needed for the imaging process.
- The additional resources required for re-planning if needed.
- The back-up imaging systems available in case of breakdown.

Questionnaire to clinics

In this section we will present the results of a questionnaire (Appendices B and C) sent to a set of clinical centres that are using 3DCT-IGRT solutions of different vendors in their clinical routines. The intention of the following data collection is to provide potential IGRT users with feedback from clinics that routinely perform 3D-patient positioning directly prior to treatment. As typical clinical cases, a head and neck treatment and a prostate treatment were selected. For each of the following systems, TomoTherapy MV CT, SIEMENS MV cone-beam CT, and kV cone-beam CT equipment from VARIAN and ELEKTA, the data that characterize the main IGRT workflow and the employed imaging parameters were collected from 3 to 5 representative clinical centres. This questionnaire can be used as an audit tool. Some of the participating centres have used it when initiating or incorporating new technology and found it useful.

The reader should be aware that the following analysis does not and cannot aim to rank and evaluate any of the technical systems in terms of their clinical usefulness. It merely focuses on workflow issues and employed imaging parameters. Naturally, a collection of data originating from clinics with different treatment strategies

and protocols will exhibit quite a variance in their specific answers to the questions asked. Furthermore, some of the questions might have been interpreted differently by individual clinics. These natural sources of uncertainties of the presented data are unavoidable and will be addressed if they seem to significantly influence the outcome of the data averages. However, despite these uncertainties we believe that the following compilation of data fairly well reflects the first experience of 3DCT-IGRT patient positioning in a clinical environment.

The workflow was divided into six sections: preparation of the imaging procedure, image acquisition, image processing (reconstruction), image registration with the planning CT, execution of patient repositioning and continuation of the treatment. For each of these steps of the IGRT procedure the participants of the study were asked to specify the time spent for three actual treatments of both clinical indications. Furthermore, the practical settings for the imaging equipment that guarantees a sufficient image quality for the intended patient set-up-correction were recorded.

In the section to follow, a summary of the results from the circulated questionnaires is shown with the full set of results provided in Appendix C. It is important to note that the results reflecting the time spent on a specific procedure in the considered workflow will depend not only on the equipment used but also on local habits and preferences within the involved institutions. Herein, we will present the major trends observed by the data obtained.

Tonsillar cancer case

Considering the overall time for the workflow, starting with image preparation and ending with the start of the actual treatment, the average time spent with the different types of equipment was as follows: TomoTherapy 11 min, VARIAN and ELEKTA each with 4.5 min and SIEMENS 7.5 min. Please see Appendix C for the range of results for each individual stage of the process. In the following we will briefly discuss where in more detail the differences in time arise from and what imaging parameter sets were employed.

Image preparation/imaging acquisition time/image acquisition parameters

First, one has to notice that the combined times for image preparation and image acquisition differ significantly between the fan-beam CT of TomoTherapy with 5 min and the cone-beam approaches of VARIAN, ELEKTA and SIEMENS with 2.5 min, 2 min and 2.5 min, respectively. The slight time advantage of ELEKTA among these seems to be related to the fact that almost all participating ELEKTA centres acquire their projections in a short scan (260–110°), while all participating VARIAN centres and two of the SIEMENS users acquired a full set of projections taken over a gantry angle of 360°.

As expected, the imaging protocols for the various 3D-imaging modalities are different. For the MVCT of TomoTherapy the only parameter that can be selected is slice thickness (course, normal, fine). However, no specific data were given in the answers. For

the Siemens MV CBCT an average of 5MUs for a 6MV beam was utilized for the complete image acquisition. One striking difference in imaging protocols, obviously related to the image acquisition mode of either short scan or full scan, was observed between the 2 kV CBCT solutions. ELEKTA centres preferred an imaging protocol with 110 kV, 10 mA, 10 ms and 360 frames for a short scan resulting in total charge of roughly 36 mAs. In VARIAN centres, however, a full scan based on the parameters 125 kV, 80 mA, 15–25 ms for 630 frames lead to an increased complete charge ranging from 756 to 1260 mAs. The conversion of the various imaging protocols to known reference values of absorbed dose can be found in the report of AAPM Task Group 75 [73].

Image reconstruction/image processing/table correction procedure

Image reconstruction time, i.e., the time measured from the end of image acquisition to the end of the image reconstruction, ranged from 5 to 35 s for different vendors, where an image cube of 256^3 voxels was generated. One centre using a SIEMENS MV cone-beam CT reported a longer image reconstruction time of 4 min for a resolution of 512^3 voxels. The main time differences observed for the different vendors are related to image registration and decision making. This step in the IGRT workflow took on average 2.5 min for the MVCT of TomoTherapy, 1 min for the kV – cone-beam CTs of ELEKTA and VARIAN and 2 min for the MV CBCT approach of SIEMENS. For the table correction and time after table correction the following values in the range of 30 s–2 min were reported: VARIAN (30 s), ELEKTA/SIEMENS (1 min), TomoTherapy (2 min).

Prostate cancer case

Regarding the complete IGRT procedure for the positioning of prostate patients the following average time requirements for the different modalities were reported: MV CT of TomoTherapy (10 min), VARIAN kV CBCT (7 min), ELEKTA kV CBCT (5.5 min), SIEMENS MV CBCT (5.5 min). Please see [Appendix C](#) for the range of results for each individual stage of the process pathway.

Image preparation/imaging acquisition time/image Acquisition parameters

Similar to the tonsillar cancer case, the reported combined image preparation and image acquisition time is the highest for TomoTherapy with 4.5 min compared to 3 min for VARIAN and ELEKTA kV CBCT and 2 min for the MV CBCT of SIEMENS. The kV-imaging protocols of ELEKTA and VARIAN centres were similar with 120–125 kV, 40–80 mA and 630–650 frames taken for 40 ms leading to complete average mAs values of 1050–1260 mAs. For the SIEMENS MV CBCT an increased number of 5–8 MUs required for imaging was reported.

Image reconstruction/image processing/table correction procedure

Not surprisingly, the same trend as in the tonsillar cancer case was observed again. The main time component in this step of the workflow is related to image registration and decision making. The shortest image reconstruction and image processing time of 1.5 min were reported by ELEKTA centres followed by SIEMENS with 2.5 min, TomoTherapy with 3 min and VARIAN with 3.5 min. For the table correction and time after table correction the following values were reported: VARIAN (30 s), ELEKTA/SIEMENS (1 min), TomoTherapy (2 min).

Perspectives

What clinical impact has IGRT demonstrated?

The rationale of image-guided strategies irrespective of its methodology is to improve the risk/benefit ratio in favor of the patient,

which may manifest as either improvement in local tumour control leading to increase in overall survival, or a reduction in treatment-related side-effects leading to maintenance or improvement in quality of life indices. With the advent of radiotherapy technology, allowing evaluating and quantifying inter- and intra-fraction temporal-spatial variability of the target volume and adjacent organs at risk, it is important to define the potential impact on patient outcomes as this will remain the true measure of its clinical value.

In this review, we have concentrated only on aspects of 3DCT-IGRT systems. This field of interest continues to undergo substantial development. At the time of writing this review, there are yet no randomized clinical trials evaluating the benefit of this technology to patient outcomes. These data are sorely needed as Level 1 evidence remains the stalwart of data to establish its clinical merit. However, we may infer the potential benefit from assessments of uncertainty derived from other clinical trials. Good examples are the randomized clinical trials of dose escalation in prostate cancer. Whilst these trials did not aim to address the issues of temporal spatial uncertainty, two subsequent retrospective reviews from these clinical trials have provided salutary insight into the pitfalls of ‘not’ accounting for treatment uncertainties [88,89]. These two retrospective studies report the loss of biochemical control in prostate-specific antigen (PSA) levels following prostate cancer radiotherapy when failing to account for the systematic error of a distended rectum in causing geographical miss of the prostate gland. The loss suffered due to geographical miss as a result of treatment uncertainty for this cohort of patients had almost negated the effect of dose escalation. It is clear that there is a need for image guidance to achieve the benefits of irradiation especially when dose escalation or sophisticated techniques such as IMRT are being used. Furthermore, when considering the implementation of hypofractionated extra-cranial stereotactic radiotherapy in anatomical regions with marked physiological activity such as lung cancer radiotherapy [90] or metastatic liver lesion radiotherapy [91], it is imperative that IGRT is utilized to provide reliable accurate targeting in order to maintain local control rates.

What remains to be done?

The performance and utility of 3DCT-IGRT systems is far from complete. There are many continued developments in software and hardware from both manufacturers and research centres that continue to refine and improve the functionality of these systems. Several of the pertinent issues have been raised previously in this review particularly in the workflow processes section. One current limitation remains the quality of the images when using cone-beam or MV CT images as they will not be of the same quality as conventional CT images. However, the pertinent question that needs to be raised is what quality of image or soft tissue detail is required to achieve the aim of image guidance. Radiotherapy of the head region may not require as much soft tissue detail if the aim is only to localize the skull when using frame-based stereotactic methods but are essential if non-rigid frameless methods are being utilized. Similar considerations apply to anatomical regions outside the head region where physiological activity and internal organ motion can readily cause temporal-spatial changes during radiotherapy. Another practical aspect when dealing with in-room cross-sectional imaging is to enable efficient workflow for data acquisition, image manipulation, multiplanar reconstruction, image registration and correlation, data quantification and evaluation for online use. Streamlining of this process needs careful attention to available software/hardware, departmental protocol and staff training [92].

A crucial challenge when utilizing 3DCT-IGRT imaging is to implement appropriate identification of regions-of-interest within the image sets. Image segmentation of the target volume or organs

at risk is often required for a variety of IGRT tasks, e.g. when manual segmentation is inefficient, tedious and time consuming particularly for complex radiotherapy sites such as the head and neck region. For online image guidance, efficient and reliable automated methods are needed and remain useful for offline correction strategies. Many software packages for deformable registration and automated anatomy segmentation are being developed for cross-sectional imaging and include atlas-based systems [93–95]. These algorithms are necessary for online target localization and to enable IGRT strategies such as adaptive radiotherapy. Better identification of the 4D changes of organs can aid the development of optimal organ sets to account for deformations that can support 4D dose calculations in treatment planning [96,97].

This aspect of target or organ segmentation may be considered to be different but complementary to the imaging information needed to adequately and appropriately delineate radiotherapy planning volumes for treatment planning. Often multi-modality imaging may be used and much work is ongoing here to determine and justify biological target volume as proposed in the insightful article by Ling and colleagues almost a decade ago [98]. A good example is the excellent work undertaken for clinical-imaging-pathological correlation undertaken in head and neck cancer and its potential use for adaptive biological IGRT treatment [99,100]. In dealing with 4D data, it is important to minimize the errors in delineation of the target and organs at risk. This also includes inter- and intra-observer variability. More robust methods of segmentation as well as delineation assessment are needed and this should form an integral part of the IGRT quality assurance program.

During a fractionated course of radiotherapy, it is important to define when to perform 3DCT-IGRT imaging. Does this need to be on a daily basis and is this the most appropriate method of imaging? The accumulation of 4D data can optimize the determination of treatment-planning margins. Techniques are being developed to provide appropriate PTV set-up margins in individual cases rather than basing margins on population statistics [101]. Some investigators have reported that daily imaging, irrespective of imaging method, is needed to maintain minimal systematic error but also to reduce random errors and this becomes more important when PTV margins are substantially reduced to levels of 3–5 mm [102,103]. This may also be appropriate when there are internal organs that can change substantially and impact on target position such as the rectum in prostate radiotherapy or if the changing organ is the target such as the bladder [104–107]. The use of 3DCT-IGRT imaging can provide the necessary information to correct for treatment delivery as well as to feedback to IGRT strategies such as adaptive radiotherapy methods and adaptive-predictive radiotherapy methods [105,108].

Another method to gain useful information for patient positioning, target localisation and treatment monitoring may be digital tomosynthesis. This intermediate solution lies between fluoroscopy and CBCT (kV or MV) and uses limited gantry rotation with multiple radiographs. The number of degrees spanned by the gantry rotation and acquisition will influence image resolution. Rotations of 40–80° reduce the dose delivered to the patient and the acquisition time with the major advantage of being able to permit imaging within a short breath hold [109]. A 60° acquisition requires only 10 s of breath hold which is a realistic level for a typical patient with a lung cancer to maintain. Furthermore, the high quality of images provides for potential to resolve soft-tissue contrast. This has been achieved for MV cone-beam digital tomosynthesis as well as in 4D mode [110,111]. The potential reduction of accumulated dose, taking into account intra- and/or inter-fraction organ motion, represents a necessary step towards 4D adaptive radiotherapy.

Another clinical issue is the tumour response or tumour growth during radiotherapy. Investigators have now reported that by reg-

ular imaging during treatment, they can quantify shrinkage of the GTV, for example, in lung cancer radiotherapy [112,113]. The current query is how to adapt appropriately to this clinical situation. Does this warrant a change in treatment plan? Does this suggest that treatment margins can be shrunk in accordance with the new tumour size demonstrated? Can we reliably estimate the sub-clinical extent of disease based simply on morphological grounds from the 3DCT-IGRT imaging or can functional imaging methods assist? Although IGRT methods have been developed to take advantage of this response feature, for example, adaptive lung radiotherapy [114], careful clinical studies with appropriate endpoints are still required. These issues will remain very active areas for research and will require controlled clinical trials for validation.

There is also a need to quantify the dosimetric variations that occur during radical irradiation as well as that resulting from patient set-up and treatment manipulations using image guidance. Transit dosimetry has been examined with cone-beam CT [71,115] and the opportunity for real time transit dosimetry is being investigated on some of the new 3DCT-IGRT systems [116]. The use of 3D dose cube sets at treatment delivery can provide further validation into the relative benefits of IGRT for different clinical situations. Estimation of doses from repeated 3D CT-based in-room imaging remains an issue and its potential impact on the emergence of second malignancies remains to be defined [117]. However, implementation of the 3D and 4D dose cube sets will be useful to facilitate future research and IGRT strategies.

The implementation of all these developments and opportunities should not be taken lightly. On the existing software/hardware platforms, the work process pathway needs further attention to optimize the various components for efficiency. An essential step in this is quality assurance. This is needed to provide the necessary confidence to maintain quality of care and to ensure that new IGRT developments are appropriately delivered. Recent clinical quality assurance programs have been outlined [118] but these would need constant review as infrastructure changes occur and new developments are instituted.

General issues

It is expected that there will be refinements and constant improvements for all the areas mentioned above in the near future. However, within the arena of 3DCT-IGRT systems, the development of an MRI-linear accelerator represents a very exciting development. The aim is to integrate the superior imaging capabilities of MRI with a linear accelerator. There are a few approaches to this concept [119,120]. There are many technical issues to be overcome before this becomes a practical reality but progress is encouraging.

The introduction and development of IGRT bring new challenges to the radiation oncology team. Education and training remain critical issues as roles within the treatment team may change depending on the IGRT method. It is appropriate to develop disease and site-specific strategies and to carefully evaluate them with appropriate clinical studies for validation. Implementation of any IGRT strategy will have to depend on the individual resource and expertise within departments and should incorporate a multi-disciplinary approach where the physicians, physicists and radiotherapy technologists are well integrated.

Conflict of interest

All authors confirm that there is no conflict of interest for this work. The following co-authors acknowledge research collaborations with research funding from the following sources: S. Korreman from Varian Medical Systems and BrainLab AG; U Oelfke from Siemens Medical Systems, D Verellen from TomoTherapy

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.radonc.2010.01.004](https://doi.org/10.1016/j.radonc.2010.01.004).

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